REMARKS

The above-noted amendments to claims 67, 76, 85, and 91 are respectfully submitted in response to the official action dated July 25, 2006. These amendments are fully supported in the specification, and no new matter is included therein. Therefore, reconsideration and allowance of the claims in this application is respectfully solicited.

Claims 67, 69-76, 78-88, and 91-93 have been rejected as being unpatentable over Miranda *et al.* '783 under 35 U.S.C. § 103(a). Miranda *et al.* '783 is said to teach a transdermal comprising a drug, an acrylate polymer, and a polysiloxane including selegiline, and propylene glycol and alcohols are said to be disclosed as optional co-solvents, citing column 13, lines 43-54, Table II thereof. The Examiner concludes that it would therefore be obvious to make a composition comprising an acrylate to deliver selegiline for the beneficial effect of transdermal delivery in view of Miranda *et al.* '783, which is said to also teach at least 50% butyl acrylate, which is said to render the polymer hydrophilic. In response to applicants' argument that the claims exclude low volatility solvents which remain present after drying between certain temperature ranges, the Examiner notes that such solvents are merely optional in the obvious composition. This rejection is respectfully traversed in view of the above amendments and arguments and for the reasons set forth hereinafter.

Before reviewing the details of Miranda *et al.* '783, reference is made to the above-noted amendments to claims such as claim 67. This claim thus now specifically requires that, before drying, at least one solvent be included in the solvent system, but that the solvents which are included cannot include those solvents of low volatility which are not driven off at drying temperatures of between around 200°F. Thus, like

claim 76, the system must include a solvent which does volatilize at such temperatures and is thus driven off during drying. This is clearly not the case with Miranda et '783.

Turning to that reference, the Examiner has referred to column 13, lines 43-54 and Table II of Miranda *et al.* '783 as teaching the optional use of co-solvents, namely, propylene glycol and alcohols. Turning to that portion of the disclosure, the patentees state that for drugs that act as plasticizers, such as nitroglycerine (or such as selegiline, the preferred drug in the present case), the drugs themselves can act as plasticizers. However, for drugs which are not readily soluble in the polymer system, it is stated that a co-solvent can be added, including propylene glycol and others. Therefore, accepting the Examiner's position with respect to the optional nature of these solvents, it is clear that Miranda *et al.* '783 does not teach or suggest the presently claimed invention. The claims now require that a solvent system be present, and that it include at least one solvent, which, however, cannot be a solvent having the low volatility and specific temperatures required thereby. As the Examiner has stated, Miranda *et al.* '783 teaches a system with no solvent at all, or a system with the solvent set forth at column 13 thereof. The present claims, however, require that at least one solvent be present, albeit a highly volatile solvent which will be removed upon drying at temperatures of 100°F to 200°F. On the other hand, when using solvents, this patentee teaches the use of a solvent system such as propylene glycol, which is specifically excluded from the present claims. Again, it is clear that the Miranda *et al.* '783 patent does not teach, suggest or disclose the presently claimed invention, including the solvent system required by these claims.

It is further noted that claims such as claim 67 are not limited to acrylic polymers, but are directed to a broader

class of polymer systems. Thus, when Miranda *et al.* '783 discloses an embodiment in which plasticizing drugs such as nitroglycerine, or selegiline, are used which might not require any solvents at all, the significance of this failure of the teachings in Miranda *et al.* '783 becomes more apparent. Thus, utilizing systems other than acrylate polymer systems, it might well be necessary to include solvent systems such as those disclosed and claimed in this application in connection with such drugs. Clearly, Miranda *et al.* '783 fails to recognize this fact by teaching either the use of no solvents at all, or the use of co-solvents, including propylene glycol, which are excluded from the present claims and whose presence would prevent one from realizing the results obtainable herewith. All of this further emphasizes the patentable nature of the present claims, and reconsideration and allowance of those claims is therefore respectfully solicited.

Applicants will not reiterate at this point all of the other reasons why Miranda *et al.* '783 does not teach or suggest the present invention, as set forth in applicants' prior response. These are merely referred to at this point, since on the above basis alone it is clear that the presently pending claims distinguish thereover.

Claims 67, 69, 70, 72, 73, 76, 78, 79, 81, 82, 85-88, and 91-93 have been rejected as being unpatentable over Sablotsky under 35 U.S.C. § 103(a). The Examiner contends that Sablotsky teaches a transdermal comprising an acrylate polymer, synthetic rubber and a crosslinking agent with specific amounts specified, and polyisobutylene disclosed as a rubber, with nitroglycerine as a liquid specified as the drug. Optional co-solvents, including propylene glycol and alcohols, are said to be disclosed at column 7, lines 58-65. The Examiner thus concludes that it would be obvious to make a composition comprising an acrylate to deliver a drug for transdermal

delivery in view of Sablotsky. In response to applicants' argument that the claims exclude low volatility solvents which remain present after drying at certain temperatures, the Examiner again notes that such solvents are merely optional in the obvious composition. This rejection is respectfully traversed in view of the above amendments and arguments and for the reasons set forth hereinafter.

Applicants would initially reiterate the positions already presented with respect to the overall nature of Sablotsky. However, in view of the above-noted amendments, it is again noted that the claims specifically require that a solvent be present, but that the solvent which is present is not a solvent which is of low volatility, and which is not driven off during drying at the temperatures set forth in the claims.

Once again, as was the case in connection with the Miranda *et al.* '783 patent, the disclosure in Sablotsky is quite similar to that in Miranda *et al.* '783. At column 7, lines 58 *et seq.*, it is again noted that with drugs such as nitroglycerine which can function as a plasticizer there might be no solvent necessary, but with other drug molecules a co-solvent, including propylene glycol and the like, can be added. Thus, this same disclosure as in Miranda *et al.* '783 leads one to the same conclusion; namely, that there is no teaching or suggestion in this reference to employ a solvent system which includes at least one solvent, but where that solvent does not include a nonvolatile solvent as defined by these claims.

Claims 1-3, 5, 8-10, 12-15, and 18-28 have been rejected as being anticipated by Lhila *et al.* The Examiner contends that this reference teaches a transdermal comprising a pressure-sensitive adhesive such as the Gelva 788 disclosed in applicants' specification, with the amounts of polymer and 0.5-15% each of triethanolamine and glycerol or polyalkylene

glycol. Propylene glycol is said to be specified and 10-60% active is said to be disclosed. In response to applicants' arguments, the Examiner contends that the properties of the claimed solvents must be possessed by the anticipatory composition because it is the same as that claimed and that applicants merely deny this proposition on its face. This rejection is respectfully traversed in view of the above amendments and arguments and for the reasons set forth hereinafter.

Applicants have previously argued in some detail that the Lhila *et al.* reference does not demonstrate a recognition of the inventive concept underlying claims such as claim 1. The Examiner, on the other hand, contends that this is irrelevant since specific permeation enhancers are disclosed in Lhila *et al.* which appear to meet the requirements of the elements in claim 1 of this application, and therefore the claim must be anticipated. Since, however, the above amendments to claim 1 now make it clear that claim 1 is no longer anticipated by Lhila *et al.*, all of applicants' prior arguments with respect to the overall nature of the teachings in Lhila *et al.* make it abundantly clear that a legitimate allegation of obviousness cannot be applied to these claims.

Claim 1 has been amended to include the limitations of prior claims 24 and 25 requiring that the amount of biocompatible deprotonating agent must be at least a stoichiometric amount compared to that of the pharmaceutically active agent, and must be sufficient to substantially completely deprotonate the pharmaceutically active agent. That this is clearly not the case either in fact or by recognition in Lhila *et al.* cannot be disputed. The only disclosure in this regard is in the examples, in which Samples I, II and III are set forth in column 3 *et seq.* of Lhila *et al.* It can be seen in this

regard that the amount of the trolamine component is approximately 1/10 of the amount of PPA utilized in these examples. (*See* Samples I and II.) On the other hand, in accordance with the present invention, as shown for example in Example 4 herein, the relationship of the deprotonating agent to the active agent is about 1:1, again with an amount sufficient to stoichiometrically convert substantially all of the active agent into the deprotonated form. (*See* also Examples 5-8 hereof.)

It is therefore clear that, even if one could say that Lhila *et al.* did disclose one compound, Tromamine 85NF, which could qualify as a deprotonating agent in accordance with the present invention, the disclosure of Lhila *et al.* regarding use of compounds which are permeation enhancers and which are pH control additives certainly does not obviate the present claims, requiring the use in general of the present deprotonating agents in amounts which are at least a stoichiometric amount compared to the amount of active agent, and which are sufficient to substantially deprotonate same. Since this is not an object of Lhila *et al.*, it cannot be obvious to do so.

In all other respects, applicants repeat their prior contentions with respect to the clear deficiencies of the Lhila *et al.* reference, but in view of the above-noted amendments to claim 1 it is respectfully submitted that at least amended claim 1 and the claims dependent thereon are clearly patentable over Lhila *et al.*, and withdrawal of this rejection is therefore respectfully solicited.

Claims 1-9, 11-14, 16-28, 67, and 69-84 have been rejected as being unpatentable over Wolter *et al.* under 35 U.S.C. § 103(a). The Examiner contends that Wolter *et al.* teaches a transdermal comprising an adhesive, a drug or salt,

and when the salt is present, an element containing basic groups. Selegeline is said to be disclosed at column 3, line 44, and ethyl acetate is said to be specified at column 4, line 64. Glycerol, an optional solvent, is said to be disclosed at column 2, line 55, and DURO-TAK 2516, disclosed in applicants' specification, is said to be disclosed therein. Eudragit E is also said to be disclosed at column 5, lines 1-3, and ethanol is disclosed at column 5, lines 10-11. The Examiner thus concludes that it would be obvious to one making a composition of selegeline and an acrylate polymer to achieve the beneficial effect of transdermal delivery in view of Wolter *et al.* As to the claimed acrylate polymer, deprotonating agent, drug and solvent, it is said to be argued that the composition is achieved when the drug and solvent of Wolter *et al.* enter the matrix of DURO-TAK 2516 and Eudragit E and that as to the claimed percent ranges of acrylate, nonaqueous solvent and drug, Wolter *et al.* is said to teach suitable amounts. Without a showing of criticality, the optimum suitable amounts are said to be obtainable by routine experimentation.

In response to applicants' arguments regarding the high and low volatility solvents being present in the obvious composition, the Examiner contends that low volatility solvents are optional and that, in any event, the high volatility solvents are ultimately removed, and applicants are said to argue but not to disclaim two layers. This rejection is respectfully traversed in view of the above amendments and arguments and for the reasons set forth hereinafter.

In responding to the rejection based on Wolter *et al.*, it is first noted that this reference is no better in its teachings of the present invention than are the Miranda *et al.* '783 and Sablotsky patents discussed in detail above. Once again, even in the context of the five-layer device of Wolter

et al., the Examiner relies upon the contention that the lower volatility solvents which are disclosed in Wolter *et al.* are "optional." Thus, all of applicants' prior contentions with respect to the clear distinctions over the same teachings in Miranda *et al.* '783 and Sablotsky certainly apply with at least equal force in this case.

Turning to the overall disclosure in Wolter *et al.*, applicants have previously pointed out that this reference specifically discloses that when a salt of the drug is utilized, the ability for it to diffuse may be improved by concomitant use of a conventional solubilizer "such as glycerol 1,2-propanediol, the monomethyl or monoethyl ether of diethylene glycol, 2-octyldodecanol, the laurate, palmitate, stearate or oleate of sorbitol, C_8/C_{10} ethoxylated glycerides, and ethoxylated oleic glycerides." (*See* col.2 ll.54-58.) Applicants thus previously stressed that, particularly with respect to claims such as claim 67, this patentee not only fails to disclose compositions substantially free of low volatility solvents which are not driven off during drying, but, to the contrary, actually requires that such solvents be incorporated into their system. At this point, however, in view of the above-noted amendments to claims such as claim 67, in which it is now required that at least one solvent be present, but that that solvent system nevertheless be substantially free of any of these low-volatility solvents, it is clear that the "optional" nature of the teaching in Wolter *et al.* does not result in the claimed product. Thus, with these optional solvents, either they are not present at all, in which case the use of the solvent system required by these claims is not suggested, or the solvents are present but they include the low-volatility solvents which are excluded from these claims. Furthermore, when Wolter *et al.*, at

column 3 thereof, describes his second layer (b), applicants once again urge that this composition includes compounds which would not meet the limitations of the present claims, including the very same nonvolatile solvents which are specifically excluded by the present claim language. It is, therefore, respectfully submitted that all of these claims are clearly patentably distinguishable over this reference, and reconsideration and allowance of these claims is respectfully solicited.

With respect to the impact of Wolter *et al.* on claims such as claim 1, reference need only be made to Example 1, the only example in Wolter *et al.* In this example, selegeline in protonated form is employed in step 1.1, but the remaining steps in this method of preparation do not include any step in which a nonvolatile amine or any other materials are used which could possibly be defined as a biocomparable deprotonating agent strong enough to essentially deprotonate the pharmaceutically active agent without causing irritation upon prolonged exposure to the skin. It is, therefore, clear that this reference also does not render claims such as claim 1 obvious, and reconsideration and allowance of these claims is also respectfully solicited.

Claims 1-14, 17-21, 24-28, 67, 69-111, and 113-119 were rejected as being unpatentable over Mantelle *et al.* '022 under 35 U.S.C. § 102(e). After stating that Mantelle '022 teaches a transdermal system with a liquid active and a polymer in which DURO-TAK 87-2852 is said to be disclosed, it is noted that selegeline is disclosed at column 3, line 6, propanalol is specified and that propylene glycol is disclosed at column 5, line 67. Rubber and polysiloxanes are said to be disclosed as well as the percentages of acrylate and drug, and ethanol and

ethyl acetate are said to be disclosed. In response to applicants' arguments that this rejection had been overcome with a declaration under Rule 131, the Examiner responds that this argument is moot since the declaration which was supplied was a copy of that directed to the parent rather than an original directed to the instant application.

While applicants submit that the facts set forth in that prior declaration are clearly applicable to the present case and to the present invention, applicants have prepared a new declaration under Rule 131, and that declaration is submitted herewith. This declaration is specifically directed to the present application, and describes the reduction to practice of the presently claimed invention prior to the effective date of Mantelle '022, and now must be admitted to eliminate Mantelle '022 as a reference hereagainst. Therefore, at the very least, withdrawal of this rejection is respectfully solicited.

Finally, claims 67-75, 94, 95, 101, 102, 105-111, 113, 115, and 119 have been provisionally rejected on the basis of obviousness-type double patenting with respect to claims 84, 86-94, and 68-80 of co-pending Application Serial No. 08/883,075 and 09/754,909, respectively. The claims are said not to be patentably distinct from each other because the present claims encompass the '075 claims regarding the presence of additional unspecified essential ingredients, and the patented claims and the '909 claims are said to encompass the present claims regarding the scope of the alkyl acrylates. The Examiner points out, however, that this a provisional obviousness-type double patenting rejection because the conflicting claims have not, in fact, been patented. It is noted, however, that as of the present date the '909 application has actually issued as U.S.

Patent No. 7,070,808 on July 4, 2006. Thus, assuming that the Examiner repeats this obviousness-type double patenting rejection with respect to this patent, applicants are prepared to file a terminal disclaimer in order to overcome this obviousness-type double patenting rejection. Similarly, since the '075 application is also expected to issue shortly, a similar offer to file a terminal disclaimer with respect to a patent which issues based on that application is also made at this time.

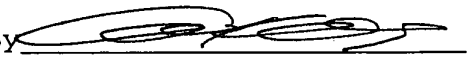
Again, appropriate disclaimers will be prepared and filed at an appropriate time during the prosecution of this application.

It is once again respectfully submitted that all the claims of this application are now in condition for allowance, and such action is therefore respectfully solicited. If for any reason, however, the Examiner does not believe such action can be taken at this time, it is respectfully requested that the Examiner telephone applicants' attorney at (908) 654-5000 in order to overcome any further objections which may exist to the allowance of these claims.

Finally, if there are any additional charges in connection with this requested amendment, the Examiner is authorized to charge Deposit Account No. 12-1095 therefor.

Dated: October 26, 2006

Respectfully submitted,

By 

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